Neurosexology
Guidelines for Neurologists
European Federation of Neurological Societies Task Force on Neurosexology*
P.O. Lundberg, C. Ertekin, A. Ghezzi, M. Swash and D. Vodusek

© 2001 EFNS

Search strategy
Four of the members of the task force have reviewed this topic in recent years: Sexual dysfunction in patients with neurological disorders (Lundberg, 1992); Sexology (Lundberg, 1994); Sexual dysfunction in selected neurological and endocrinological disorders (Lundberg, 1997a); Diabetes mellitus and sexual dysfunction (Ertekin, 1998); Neuro-physiological tests in erectile dysfunction (Vodusek, 1998); Clinical neuro-physiology – in bladder, bowel and sexual dysfunction (Vodusek and Fowler, 1999); Physiology of female sexual function and effect of neurological disease (Lundberg 1999); Sexual rehabilitation (Fugl-Meyer et al. 1999); Sexuality and multiple sclerosis (Ghezzi, 1999); Neurological disorders: Erectile and ejaculatory dysfunction (Lundberg et al. 2000). Further details on clinical neurosexology can be found in these reviews. The members of the task force are all familiar with neurosexological issues in their clinical work. Besides commonly used search strategies in standard databases (such as Medline and PubMed, which, however, are not very complete with regard to sexological references) many other databases, public and private, have been used. Members of the group have been searching references pertinent to the field of neurosexology since the mid-1950s. Exerpta Medica, Neurology/Psychiatry/ Gynecology/Urology were used for many years. Since the appearance of Current Contents this journal have been used and in recent years Index Medicus, Medline and for the last couple of years NCBI PubMed through http://www.ncbi.nlm.nih.gov. Language has not been restricted. The sexological terms most frequently used have been: sex, sexology, sexuality, sexual behaviour, sexual function, sexual dysfunction, desire, libido, erection, erectile dysfunction, ejaculation (absent, retarded, retrograde), orgasms, anorgasmia, lubrication, priapism. In this review only selected references are given, mainly in English, and mainly from the last 25 years. For review of earlier literature, the reader is referred to reviews by Lundberg (1980, 1992, 1997a).

It should be observed that in the literature the sexual symptoms and problems of patients with neuro-
logical disorders are often poorly described and defined and can hence be misinterpreted.

Result of literature search

The sexual response phases

Based on their observations of human sexual behaviour in a laboratory setting, Masters and Johnson constructed a model of the sexual response cycle comprising four different phases: Excitement, Plateau, Orgasm and Resolution (EPOR; Masters and Johnson, 1966). According to their model, sexual desire is not a phase in itself. This model has reached a wide public and is used in most textbooks on sexual physiology. However, their observations, although pioneering, were not well controlled and quantified, and their four-phase model has been criticised. Kaplan (1974) has simplified the sexual response model into three phases: Desire, Excitement and Orgasm (DEO). This model fits better with physiological observations in human males and also with animal research. On the other hand, it has become more and more evident that from the psychological point of view female sexuality is much more complex (Basson 2000). From sexual neutrality, the woman may be seeking for human attention and stimuli for non-sexual reasons. This leads to an arousal that may include a physiological genital response which in turn starts a sexual response cycle with awakening of sexual desire and so on. Thus, one could talk also about a phase of foreplay (‘FDEO’). It is also important to understand that sexual arousal directly or indirectly results in further stimulation which gives rise to more arousal and so on, thus working as a circuit mechanism.

Viewed from a neurological point of view, the sexual response involves a series of neurally controlled phenomena occurring in a hormonally defined milieu. The behaviour comprises different components: motivation, arousal, genital reactions (erection, lubrication, emission, ejaculation) and orgasm. Obviously, all have their neuroanatomical, neurophysiological, neurochemical, and neuropsychological dimensions, but only the visual reactions in males have been extensively explored to date. The genital components are therefore the focus of discussions on sexual dysfunction, and few controlled data are available on other physiological aspects of sexuality. Essentially reflex in nature, the sexual response has a definite major psychological dimension, and can be significantly influenced by neuropsychological factors.

Viewed from a functional point of view, and limiting ourselves to the male genital components of the normal sexual functioning, the erection has to be firm enough for vaginal penetration, and the level of rigidity has to be maintained through intercourse to bring about ejaculation, which in turn should deliver sperm to the uterine cervix. The male sexual response cycle has been extensively studied. Our knowledge about the female response cycle is much less complete. A recent review gives more details (Levin, 1998).

Basic sexual anatomy and physiology

It is beyond the purpose of this review to discuss the details of genital anatomy. Genital innervation is both somatic and autonomic. Somatic sensory afferents deliver information on tactile sexual stimuli, which induce local sexual responses (vascular–erectile and glandular) after synapsing in the sacral spinal cord. Sensory information is projected to suprasacral regions and is important in other reflex activity, leading to awareness and sexual excitation. Parasympathetic efferents travelling through the pelvic plexus and the greater and lesser cavernosal nerves initiate the erectile response. The blood flow in the penile artery increases, Smooth muscles lining the cavernosal sinuses in the penile corpora become relaxed. Helicine arterioles branching from cavernosal arteries selectively shunt blood flow to the lacunar spaces of the cavernosal bodies, which fill with blood; subtunical venules become compressed. Intracorporeal pressure increases and then stabilizes at a level approximating systolic blood pressure and causes penile tumescence and rigidity. Continued parasympathetic activity maintains this erection (Smith and Bodner, 1993). This parasympathetic pathway is, however, not the only proerectile pathway: erections are observed in humans and experimental animals after lesions of sacral cord segments and pelvic nerves. The best candidates for this alternative proerectile pathway (leading to the so-called psychogenic erections in paraplegics with conus or cauda equina lesions but preserved thoracolumbar segments) are the hypogastric nerves. Their role is to some extent still controversial and may be different in different species.

Continued stimulation eventually triggers orgasm with seminal emission, rhythmic phasic contractions of perineal and pelvic floor muscles, and ejaculation of urethral contents. Actually emission begins during arousal (Mitsuya et al., 1960). Ejaculation is effected by integrated sympathetic outflow from T11–L2 segments travelling through the sympathetic chain, the hypogastric plexus and along pelvic and pudendal nerves (Giuliano et al., 1995), and somatic efferents travelling through pudendal nerves. Animal experiments have shown cross-innervation of the peripheral sympathetic nervous system (Kihara and Degroat, 1997). Thus,
nerve fibres running in the left mesenteric plexus go to the pelvic plexus on both sides and innervate vas deferens on both sides, and vice versa. Sympathetic outflow causes smooth muscle contraction: in seminal vesicles, vas deferens, the prostate (to deliver seminal fluid to the posterior urethra); in the bladder neck (to prevent retrograde ejaculation); and in the corpora cavernosa, to cause detumescence. The latter ‘antierectile’ activity is probably inhibited during erection through spinal coordination of reflex action. In the periphery, the main proerectile transmitter has been shown to be NO (nitric oxide), which is colocalized with VIP (vasoactive intestinal peptide) and acetylcholine. The main antierectile neurotransmitter is probably noradrenaline (Giuliano et al., 1995). Although the predominant neural control of the male accessory sexual organs is sympathetic (adrenergic and purinergic), there is probably also parasympathetic control over the secretion of fluids that contribute, overall, to seminal fluid (Hoyle et al., 1994). Appropriate sensory stimulation leading to erection and orgasm is not necessarily purely genital, and erections caused by stimuli delivered through cranial nerves might also be reflexive, although this is usually subsumed under ‘psychogenic’ (Sachs, 1995). Mental imagery is the ‘real’ psychogenic descending activating stimulus of these spinal cord-integrated reflex responses.

The pattern of genital neuromuscular activation is thought to be similar in women, in whom parasympathetic activity causes clitoral erection, engorgement of the labia, and vaginal lubrication. Orgasmic sympathetic activity results in contractions of uterus, fallopian tubes, and paraurethral glands, and somatic motor activation causing rhythmic contractions of pelvic floor muscles (Bérard, 1989).

The spinal cord organization of the reflex coordination involved in human sexual responses remains to be elucidated. Spinal cord sites concerned with cavernosal smooth muscle control have been localized to preganglionic autonomic nuclei in both thoracolumbar and lumbosacral segments in the rat (Marson et al., 1993). Genital afferents probably synapse, via interneurones, with both somatic and autonomic motoneurones; those projected to supraspinal structures travel in the anterolateral funiculus. Both thalamic and cortical areas receive sensory input from the genitalia, and sexual feelings may be elicited when such areas are stimulated. In the primary sensory cortex the genitalia are represented in the parasagittal area (Penfield and Jasper, 1954). In studies using retrograde labelling in the rat, as revealed by the transneuronal transport of pseudorabies virus, most of the labelling from corpus cavernosum at the level of the brainstem was in the pons and medulla (Marson et al., 1993).

Descending projections from the brainstem raphe nuclei travel in the lateral funiculus. The nucleus paragigantocellularis was shown to have a majority of serotoninergic neurones that project to the spinal cord and provide tonic inhibition of sexual reflexes in the rat (McKenna et al., 1991).

In the diencephalon, the labelled neurones, after injection of pseudorabies virus in the corpus cavernosum, were found only in the hypothalamus, especially the paraventricular nucleus, the tuberal region, the medial preoptic area, and the dorsal hypothalamic area (Marson et al., 1993). Neurones from the paraventricular nucleus project to the thoracic and lumbosacral nuclei concerned with erection. Hypothalamic spinal projections are situated in the dorsolateral funiculus (Giuliano et al., 1995). The hypothalamus is also directly involved in the control of the gonadotropic functions of the pituitary and thus the prenatal development of the genital organs, pubertal development, and the menstrual cycle. In the basal hypothalamus, there is a region important for sexual desire, which is affected by tissue levels of the sex steroid hormones (testosterone, dihydrotestosterone and oestradiol).

Animal experiments have delineated a dopaminergic stimulating and a serotoninergic inhibiting mechanism controlling sexual desire. Furthermore, the human sexual desire is influenced by psychic factors. Androgens are necessary but apparently not essential for normal desire (Kwan et al., 1983). Sexually dimorphic nuclei are localized in the anterior hypothalamus in the preoptic region. The medial preoptic area seems to be of particular importance in regulating sexual motivation and performance, and dopamine may regulate penile erection at this level. Cortical and subcortical structures related to the limbic system, particularly the hippocampus, have been shown to elicit erection when stimulated (in monkeys; Dua and MacLean, 1964). Overall, the role of the cerebral hemispheres, the rest of the brain, and even of the spinal cord in controlling sexual behaviour is far from being fully elucidated. It is suggested that the brain has an overall inhibitory influence on sexual behaviour, which, at least as far as genital reflexes are concerned, is organized at the spinal level, where proerectile and antierectile activity is balanced to achieve an appropriate erection, and then emission is integrated with ejaculatory mechanisms to provide semen to the cervix of a female. Particularly important unsolved questions related to diagnostic concepts of erectile dysfunction are whether psychogenic and reflex erections are as differentiated as commonly presumed, and whether sleep-related erections have identical neural control mechanisms to sexually elicited erections.
Case history in patients with sexual dysfunction and neurological disorders

General aspects
From the general medical point of view the case history should include a survey of the patient's medical history, particularly concerning cardiovascular, endocrine, psychological and psychiatric disturbances, neurological disorders, disorders of the sex organs, prior trauma and surgical procedures, the use of prescription drugs, smoking and alcohol habits, and drug abuse.

Detailed history related to sexual dysfunction
From the sexological point of view, the case history should define the patient's sexual expectations, needs and behaviour and should identify sexual problems as well as misconceptions. Psychological factors are frequently involved, either as an emotional reaction to sexual dysfunction or as a consequence of a socially or physically disabling disease. Dependence and lack of acceptance of the sexual disorder by the patient or the partner, self-perceived unattractiveness and reduced self-esteem also play a relevant role. It is usually important also to interview the partner (if the patient has one) and to evaluate the quality of the marital/partner relationship.

To summarize, it is important to clarify the nature and the characteristics of sexual dysfunction, to discover any underlying (and possibly treatable) organic cause and to document the existence of primary or secondary psychological factors.

Details of the case history of particular neurological interest
As always in neurology, chronology is very important. Has the problem been there all the time, or did it have an onset at a particular time? Was the onset rapid or gradual, the course progressive or episodic?

1. The patient should be asked about sexual desire. Is there a complete lack of desire? Does the patient not experience spontaneous sexual desire but wishes to have it or is the desire easily evoked by ordinary situations? Do any particular stimuli, whether visual, tactile or emotional play an important role? Is the desire partner-dependent or not? The term Hypoactive Sexual Desire Disorder (HSDD) is sometimes used. HSDD can be defined as the persistent or recurrent deficiency or absence of sexual fantasies, thoughts, desire for sexual activity, alone or with a partner, and inability to respond to sexual cues that would be expected to trigger responsive sexual desire. To be significant, these symptoms need to be causing personal distress (Basson 2000).

2. Sensory aspects of sexual function should be elicited. The patient should describe sensory experiences of sexual arousal in different parts of the body. Present or past disturbances of sensitivity in the region corresponding to the sacral segments are of particular interest as well as pain during sexual arousal or intercourse, and pelvic or superficial dyspareunia.

3. Descriptions of erections are important. Does the patient have nocturnal erections, morning erections, erections evoked by visual, auditory or psychogenic stimuli and erections evoked or enhanced by genital stimulation? What is the quality of penile tumescence? Is erection sufficient for penetration? Is there a premature loss of erection during sexual intercourse? Does the patient have episodes of priapism or painful nocturnal erections? Women should be asked about erections of the clitoris and vaginal lubrication. Are these female reactions evoked by visual, emotional or direct genital stimulation?

4. Ejaculation should be described. Does the patient have premature or retarded ejaculation, or even absence of ejaculation (anejaculation)? Is the ejaculation dribbling, i.e. are there emissions of semen through the urethra without contractions of pelvic floor muscles? Retrograde ejaculation means ejaculation into the bladder with presence of spermatozoa in urine. Aspermia means lack of emission of semen. Both can be described as dry ejaculation. The fertility history should be investigated. Is there urinary incontinence during sexual intercourse or does the female have forceful ejaculation of fluids from the urethra during orgasm (so-called female ejaculation)?

5. Orgasms should be described. Orgasm can be defined as the sum of all physiological events that happen in the body during the sexual climax and how this is experienced by the individual. Others define the orgasm solely as the feeling of sexual pleasure. What is the capacity to achieve an orgasm? Does the person (male or female) actually feel the pelvic floor muscle contractions? How is the quality of orgasmic sensations and experiences? An orgasm may be also anhedonic, i.e. without pleasurable sensations. Spontaneous orgasms do also occur and orgasms may be painful.

6. Menstrual function should be delineated. How old was the woman at first menstruation? Has menstruation been regular? When was the last menstruation? Are menstruations painful (dysmenorrhea)?

Formal questionnaires can be used to obtain standardized information. Frequently used forms are the Brief Male Sexual Function Inventory for Urology (O’Leary et al., 1995) and The International Index of Erectile Function (IIEF, 1997). It has been suggested that these protocols are helpful in studies of treatment efficacy in patients with erectile disorders, but not
practical for everyday assessment of patient with sexual dysfunction (Lue, 1996).

**The clinical examination of the patient with sexual dysfunction**

Guidelines for the neurological evaluation of male sexual dysfunction have also been given by the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology, 1995.

**General clinical examination**

Sexual development, body length and weight, changes in pigmentation and body hair and the presence of galactorrhea are looked for. Inspection of external genitalia for any pathology, and evaluation of the size of the testes (normal 15–25 mL), the clitoris and the prostatic gland are performed. Distribution of body hair and how frequently the man in question has to shave should also be evaluated.

Palpation of peripheral pulses (arms, legs, penis), auscultation of the heart, and blood pressure measurement are mandatory.

**Neurological examination**

A standard neurological examination including assessment of the mental state should reveal any signs of an underlying neurological disease. The examination should be related to the particular problem by the patient. In addition, lower back (naevus, hypertichosis, sinus) and feet (deformity, muscle atrophy) should be carefully examined. The sacral segments are especially important. The bulbocavernous muscles can be palpated in the male, and tested for voluntary (’move the penis’), and reflex contraction. Anal sphincter and levator ani tone (pubococcygeus muscle) and voluntary and reflex contraction can be palpated in both sexes. In addition to standard reflexes the cremasteric reflex (testing the L1 segment), and the bulbocavernosus and external anal reflex (testing the S2–S4/5 segments) should be evaluated. The bulbocavernosus reflex can be elicited by squeezing the glans and assessing contraction of the anal sphincter (in both sexes) or the bulbocavernosus muscle (in males) by palpation. The external anal reflex is tested by repetitive pricking (or a scratch) delivered to perianal skin (on both sides!) and observing anal sphincter contraction. Skin sensitivity is tested for touch and pain perception in the perineum, perianal and genital skin, in addition to testing over other dermatomes.

Particular laboratory tests (usually classified as neurophysiological) are direct extensions of clinical examination of nervous function. Thus, reflex responses can be recorded with greater sensitivity electromyographically; and perineal sensation can be quantified using special devices and algorithms (see below).

**Investigations**

Generally speaking, investigations will be used to assess sexual function objectively, and then to address questions of aetiology. In selected male patients, spontaneous and physiologically induced erections are examined; other segments of sexual function (in either sex) are as a rule not directly evaluated. In males with erectile dysfunction, the capacity to obtain pharmacological erection (with alprostadil) is evaluated and basic blood and urine tests are performed. In some of these further investigation is performed to evaluate the neurogenic, vascular, endocrinological and other possible aetiological factors, but always in relation to therapeutic and prognostic considerations.

**Investigation of erectile function.** Although essential data will be obtained by history, objective evaluation of erection is considered the ‘gold standard’ to determine its quality. Spontaneous and physiologically induced erection can be studied with a variety of techniques. Spontaneous nocturnal penile tumescence and rigidity can be measured in the sleep laboratory using strain gauges (measuring penile expansion), visual inspection and measuring the buckling force (for assessment of rigidity), with polygraphic confirmation of sleep phases; such a procedure is considered the most accurate for determining erectile function (Karacan and Ilaria, 1978; Wasserman et al., 1980). Various low-cost screening tests for nocturnal penile expansion have been proposed, but their validity is questionable (Condra et al., 1987). Continuous monitoring of nocturnal penile tumescence and rigidity can be obtained by a rigidometer during normal sleeping conditions at home (Kaneko and Bradley, 1986), and also during daytime napping (Morales, 1994) or in the conscious sexually stimulated examinee (Thase et al., 1988).

Screening tests for nocturnal penile tumescence (NPT) have been classified as promising in distinguishing psychogenic from other causes of erectile dysfunction, but insufficient on their own to arrive at such a conclusion. Home measurements with the rigidometer have been classified as promising in establishing the presence and quality of erections. A comprehensive discussion on the utility and limitations of the NPT test has been given by Morales et al. (1990).

**Investigation of erectile capacity.** In addition to the need to study spontaneous or physiologically induced erections (to verify history data and distinguish...
psychogenic from organic dysfunction), the greatest advance in diagnosis of erectile failure came with the introduction of pharmacologically induced erections. Given that no major vascular problem is present (particularly no significant venous incompetence) an intracorporeal injection of a vasoactive substance (papaverine; combination of papaverine + phentolamine; prostaglandin E1) will lead to an erection, thus strengthening the suspicion of a neurogenic or psychogenic aetiology of erectile dysfunction (Mueller and Lue, 1988). The addition of self-stimulation is considered to increase test sensitivity (Lue, 1990). Intracorporeal injection of vasoactive agents has been proposed as an established diagnostic tool in patients undergoing assessment for possible neurogenic erectile dysfunction, and safe if performed by experienced physicians, with an acceptable complication rate (Haldeman et al., 1995).

Investigation of nervous system function: clinical neurophysiological and other methods. In patients with erectile (and occasionally ejaculatory) dysfunction and (suspected) neurological disorder a diagnosis of involvement of neural and muscular structures related to sexual function may be strengthened, refined and documented by neurophysiological tests. There are several different methods, classified according to the neuroanatomical subsystem whose function they test. Motor (somatic and autonomic), and sensory (somatosensory and viscerosensory) tests may be distinguished (Table 1). Most of the tests are electrophysiological, but quantitative sensory testing and testing lower urinary tract and anorectal function (as indices of sacral autonomic function) can be conveniently discussed under the same heading.

In addition to clinical testing for sensation, special devices and algorithms can be used for quantifying sensory perception on the genital organs. Measuring vibratory perception (biothesiometry/vibrametry) on the penis has been found to correlate with results of electrodiagnostic testing (Padma-Nathan, 1988). The vibration perception threshold (VPT) in the penis (glans and shaft) in a neurologically healthy man is similar to that of the feet. In females VPT is best measured in the clitoris, labia majora and perineum (Helström and Lundberg, 1992). The threshold for clitoris in neurologically healthy women is the same as in the hands. VPT is of particular importance in women with suspected lesions of peripheral sensory nerves in the pelvic floor area. The test is considered as promising in evaluating penile sensation (Haldeman et al., 1995). Even more informative on nervous control of erection should be tests evaluating small fibre function, i.e. testing for penile thermal sensation (Yarnitsky et al., 1996). In women vaginal and clitoral warm and cold sensory thresholds may be used to assess neural dysfunction (Vardi et al. 2000).

Electromyography (EMG) may be used to demonstrate activation patterns of striated muscles (within the sexual response [kinesthesiological EMG]; as for instance demonstrating the pattern of perineal muscle activity during ejaculation) (Gerstenberg et al., 1990). However, EMG is mainly used to differentiate normal from denervated (reinnervated) muscle. Concentric needle EMG can identify both changes due to recent denervation and reinnervation, and is considered the method of choice to diagnose lower motor neurone involvement in the lower sacral segments (Vodusek & Fowler 1998). Different tests involving stimulation and recording of somatosensory- and motor-evoked responses, and sacral reflexes, reflect the function of defined parts of the motor and sensory nervous system. These tests measure conduction through nervous pathways and are sensitive to demyelination, but not to axonal lesions (which predominate in clinical practice). Tests have been proposed to assess the lumbosacral sympathetic system (the sympathetic skin responses) and penile smooth muscle (the corpus cavernosum EMG). Details of methodology and findings are discussed elsewhere (Vodusek, 1998).

The demonstration of nerve or muscle pathology by these neurophysiological tests may refine the diagnosis of nervous system involvement, and the procedures are safe. These tests, however, cannot themselves define erectile dysfunction as neurogenic (Haldeman et al., 1995); the relationship of any neurophysiological test abnormality to sexual dysfunction per se has proven to

Table 1 Tests of nervous system function

<table>
<thead>
<tr>
<th><strong>Somatic sensory tests</strong></th>
<th><strong>Quantitative sensory testing</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dorsal penile nerveography</td>
</tr>
<tr>
<td></td>
<td>Pudendal somatosensory evoked potentials (SEP)</td>
</tr>
<tr>
<td></td>
<td>Measuring bulbocavernous and anal reflex latencies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Visceral sensory testing</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>SEP to proximal urethra/bladder neck stimulation</td>
</tr>
<tr>
<td>Testing bladder sensitivity</td>
</tr>
<tr>
<td>Sacral reflex to proximal urethra/bladder neck stimulation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Somatic motor tests</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Electromyography</td>
</tr>
<tr>
<td>Pudendal motor latency</td>
</tr>
<tr>
<td>Motor evoked potentials (MEP)</td>
</tr>
<tr>
<td>(above-mentioned reflexes also test the motor part of the reflex arc)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Autonomic tests</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic skin response</td>
</tr>
<tr>
<td>Penile (corpus cavernosum) EMG</td>
</tr>
<tr>
<td>Neurocardiac tests</td>
</tr>
<tr>
<td>Cystometry</td>
</tr>
<tr>
<td>Anorectal manometry</td>
</tr>
</tbody>
</table>
be elusive. However, measurements of dorsal penile nerve conduction, the bulbocavernosus reflex, and pudendal SEP have been classified as promising tools in evaluating patients with suspected neurogenic erectile dysfunction (Haldeman et al., 1995). In particular, the tests measuring penile autonomic innervation and smooth muscle function would be of value in diagnosis, but their validity is at present not fully evaluated. Cystometry, other urodynamic tests, and anorectal function tests may strengthen a suspicion of sacral autonomic dysfunction.

After delineating (as precisely as required) the presence of a neurological deficit by clinical and laboratory examination, further investigations (neuroradiological, cerebrospinal fluid, etc.) necessary to diagnose the neurological disorder are performed.

Laboratory investigation of blood and urine. Basic laboratory data (including sedimentation rate, blood cell count, fasting blood sugar, serum lipids, urinanalysis) as well as serum parameters screening for hepatic, kidney and thyroid function should be obtained in every patient suspected to suffer from organic sexual dysfunction. What hormone to be studied is dependent on the circumstances (sex, age, onset of symptoms). Prolactin and testosterone levels have been proposed as screening tests for both sexes. In females with menstrual irregularities or signs of masculinization further hormone assays may be necessary.

Investigation of vascular function. If intracorporeal injection testing of penile tumescence has strengthened a suspicion of vascular aetiology in the male patient with erectile dysfunction, further investigations may be contemplated, as a rule performed by urologists. Penile blood pressure can be measured using a simple Doppler method and then related to the arm blood pressure. Vascular competence can be measured by angiography, colour ultrasonography and dynamic cavernosography. It has been stressed that the purpose of testing should always be defined: pharmacotesting may be sufficient for the majority of patients, and the invasive tests reserved for those in whom surgery is contemplated (Meuleman and Diemont, 1995). In females, there are also a number of vascular tests available. However, their importance in clinical diagnosis of sexual dysfunction has so far not been evaluated.

Psychological testing. If the psychogenic component is considered of aetiological relevance, further to data obtained by history, and the observations made during the neurological examination, a clinical psychological assessment is useful.

Sexual dysfunction and neurological disorders

Sexual dysfunction with hypothalamo–pituitary disorders

Decreased or absent sexual desire is the cardinal symptom in males with hypothalamo–pituitary disorders. In most male cases, this is the first symptom to appear. However, males rarely seek medical advice because of loss of sexual desire. Hence, the diagnosis is usually postponed in men until some other symptom appears. The second symptom to appear is usually hypothyroidism or visual field defects. However, it may last as long as a decade after the onset of the sexual problem before any further symptom develops in a pituitary tumour case.

Studies have shown that 75% of men with hypothalamo–pituitary disorders report decreased or absent sexual desire at the time of diagnosis. The figures are higher for those with larger tumours extending into the suprasellar region than for those with intrasellar tumours. A highly significant correlation has been found between low serum testosterone levels and a decrease in desire (Lundberg and Wide, 1978). Usually the patients also have erectile failure. However, because of lack of desire this does not often present a great problem to the patient.

Decreased sexual desire is also the first symptom in most men with smaller pituitary tumours and hyperprolactinaemia (Muhr et al., 1985). Even in this group of patients, low serum testosterone is common among those with decreased desire. Probably decreased testosterone levels are more important in causing this symptom to develop than hyperprolactinaemia. However, there are some males with hyperprolactinaemia who report decreased sexual desire despite normal serum testosterone.

In women, the situation is somewhat different. Here, amenorrhoea and infertility are usually the problems that take the patient to the doctor. In females aged 20–60 years with morphologically verified hypothalamo–pituitary disorders (Hulter and Lundberg, 1994) two-thirds notice absence, or a considerable and troublesome decrease in sexual desire. This problem is much more common among women with hyperprolactinaemia than among those with normal serum prolactin. Most of these women have amenorrhoea. Problems with lubrication or orgasms are also very common in this group of women.

In most instances hypothalamo–pituitary disorder is caused by a pituitary adenoma, whether hormone-secreting or not. Less common types of tumours are craniopharyngiomas, meningiomas, optic gliomas, hypothalamic hamartomas and metastases (Lundberg, 1980). Other causes of hypothalamo-pituitary dys-
function are congenital malformations of the rhinencephalon, hypothalamus and/or pituitary such as dysplasia of the sella turcica or dystopia of the posterior lobe, ollæcto-genital dysplasia or hypogonadotropic hypogonadism with anosmia (in its hereditary form called Kallmann’s syndrome) and septo-optic dysplasia or de Morsier’s syndrome. A further group constitutes acquired disorders such as post-traumatic hypothalamic bleeding, postpartum pituitary necrosis (Sheehan’s syndrome), ruptured arterial aneurysms, sequelae of acute asphyxia, spontaneous arrested infantile hydrocephalus, delayed radiation necrosis, meningoencephalitis, sarcoidosis, histiocytesis-X (Hand–Schüller–Christian syndrome) and a great number of degenerative neurogenetic disorders. The clinical symptomatology is dependent upon the age of onset and the rate of progression. Otherwise, these disorders more or less regularly result in hypogonadism and loss of libido and potency. In rare cases (spontaneously arrested hydrocephalus and hypothalamic tumours, hamartomas in particular) precocious puberty is the cardinal symptom. However, there are many other causes of secondary hypogonadism. Thus, in a CT/MRI study of 164 impotent males with low serum testosterone values pathology in the hypothalamo–pituitary region was found in only 11 patients (Citron et al., 1996).

In a number of families with cerebellar or spinocerebellar ataxia, hypogonadism of the hypogonadotropic form, indicating a hypothalamic–pituitary insufficiency, has been found (Neuhäuser and Opitz, 1975; Berciano et al., 1982; Koskinen et al., 1995).

**Sexual dysfunction in patients with brain injuries and encephalopathies**

Disability and cognitive impairment occur rather frequently after a traumatic brain injury. Sexual impairment is not rare, as a consequence of cerebral lesions or psychological factors. Both decreased and increased sexual desire have been reported in both sexes. Little is known about female sexual arousal after traumatic brain injuries. However, in males both impotence and retarded ejaculation have been reported (Meyer, 1955; Kreutzler and Zasler, 1989). Hypersexuality or altered sexual preference may also occur after brain injuries. Sexual problems are more frequently seen in three-quarters of the females and two-thirds of the males after stroke (Sjögren et al., 1983). Sexual problems in post-stroke patients are usually explained in terms of lack of coping. Diminished sexual contact for post-stroke patients is due primarily to the patient’s overwhelming fears of inadequacy. Other psychological factors have also been suggested. Cognitive impairment may disturb the sexual part of a relationship. Sexual problems are more frequently seen in cases with aphasia (Wiig, 1973). General hemihypoaesthesia is associated with decreased sexual drive probably due to loss of erogenous zones. Hypersexuality may also be the result of a stroke (Monga et al., 1986; Donnet et al., 1997; Absher et al. 2000).

**Sexual dysfunction in patients with epilepsy**

Numerous symptoms of sexual dysfunction can be seen in epileptic patients, during the interictal period or in relation to seizures.

**Interictal phenomena.** Many men with epilepsy suffer from loss of sexual desire, reduced sexual activity, and/or inhibited sexual arousal (Saunders and Rawson, 1970; Danskj et al., 1980; Goldner and Morrell, 1996). The figures vary in different studies but are generally higher than those observed in the general population. Inability to maintain erection and, more rarely, ejaculatory dysfunction, decreased satisfaction with sexual life, reduced sexual fantasies, reduced sexual dreams and initiatives, as well as reduced orgasmic vailing symptom (Gerstenbrand and Lücking, 1971; Oliveira et al., 1989; Hayman et al., 1998). Pansexuality, that is, sexual drive directed not towards human beings but also towards animals and inanimate objects, is often a major feature. The lesions may be traumatic, sequelae of viral meningoencephalitis, complications of SLE or cancer treatment.

Sexual symptoms may also occur in non-traumatic encephalopathies, prion diseases for example (fatal familial insomnia, Montagna, 1999; sporadic Creutzfeld-Jakob disease, Lundberg, unpublished observation). Other types of dementia will not be dealt with in this review.

**Sexual dysfunction and stroke**

About three-quarters of stroke patients who have been sexually active before their stroke report abrupt and permanent decrease in coital frequency. A feeling of an overall change in sexual life is reported more frequently by male patients. The majority have erectile dysfunction after stroke (Kalliomäki et al., 1961; Sjögren et al., 1983; Monga et al., 1986; Boldrini et al., 1991; Aloni et al. 1998, Korpeilainen et al., 1998). Orgasmic dysfunction is seen in three-quarters of the females and two-thirds of the males after stroke (Sjögren et al., 1983). Sexual problems in post-stroke patients are usually explained in terms of lack of coping. Diminished sexual contact for post-stroke patients is due primarily to the patient’s overwhelming fears of inadequacy. Other psychological factors have also been suggested. Cognitive impairment may disturb the sexual part of a relationship. Sexual problems are more frequently seen in cases with aphasia (Wiig, 1973). General hemihypoesthesia is associated with decreased sexual drive probably due to loss of erogenous zones. Hypersexuality may also be the result of a stroke (Monga et al., 1986; Donnet et al., 1997; Absher et al. 2000).

About three-quarters of stroke patients who have been sexually active before their stroke report abrupt and permanent decrease in coital frequency. A feeling of an overall change in sexual life is reported more frequently by male patients. The majority have erectile dysfunction after stroke (Kalliomäki et al., 1961; Sjögren et al., 1983; Monga et al., 1986; Boldrini et al., 1991; Aloni et al. 1998, Korpeilainen et al., 1998). Orgasmic dysfunction is seen in three-quarters of the females and two-thirds of the males after stroke (Sjögren et al., 1983). Sexual problems in post-stroke patients are usually explained in terms of lack of coping. Diminished sexual contact for post-stroke patients is due primarily to the patient’s overwhelming fears of inadequacy. Other psychological factors have also been suggested. Cognitive impairment may disturb the sexual part of a relationship. Sexual problems are more frequently seen in cases with aphasia (Wiig, 1973). General hemihypoesthesia is associated with decreased sexual drive probably due to loss of erogenous zones. Hypersexuality may also be the result of a stroke (Monga et al., 1986; Donnet et al., 1997; Absher et al. 2000).
capacity, are also reported in patients with complex partial epilepsy and mesial-basal temporal lobe spike foci, but in these studies data were not compared with primary generalized epilepsy (Taylor, 1969; Shukla et al., 1979). In another study (Morrell et al., 1994) sexual dysfunction was more frequent in partial than in generalized epilepsies. Decreased sexual arousability, vaginism and dyspareunia are reported by many female epilepsy patients (Demerdash et al., 1991). Hypersexual episodes are reported in a few cases (Blumer, 1979). Most patients with low sexual desire have complex partial epilepsy and temporal lobe lesions. Sexual interest seems to be more reduced in patients with right temporal lobe epilepsy compared to patients with the left hemisphere disorders. Whether the patient has undergone surgery for their epilepsy or not does not seem to be of importance (Christianson et al., 1995). Life satisfaction and sexuality are higher in patients who are seizure-free compared to those non-seizure-free. Epileptic patients, especially males, have a lower marriage rate compared to the general population. Married female patients have fewer children than expected (Dansky et al., 1980). Social and psychological factors play an important role.

In fact epileptic patients describe poorer psychological health compared to healthy subjects. It should also be noticed that antiepileptic drugs, especially the older types (phenytoin, phenobarbital, primidone, carbamazepine and valproate), may lead to hormonal changes (particularly increased oestriadiol and decreased free testosterone levels in men), as well as decreased sexual desire and performance in both sexes (Isojärvi et al., 1995; Duncan et al., 1999). Subclinical hypogonadotropic hypogonadism caused by the brain damage has also been suggested as the explanation in some cases. It should be noticed that menstrual irregularities are common among epileptic patients (for review, see Lundberg, 1997b).

Seizures and sexual phenomena. Epilepsy and sexual behaviour may be connected in many ways. Thus, sexual activity can provoke an epileptic attack, sexual phenomena may be a part of an epileptic seizure, and the epileptic patient may display changes in sexual behaviour. Such cases have given us important insights in the sexual physiology of the human brain. (For details about sexual phenomena in epileptic patients, see Lundberg, 1992).

Hyperventilation is well known as an inducing event that can provoke a generalized epileptic seizure. Hyperventilating during sexual intercourse may sometimes provoke an epileptic fit. However, reflex mechanisms during sexual behaviour could also trigger a partial epileptic attack from the corresponding cortical area. Sexual fantasies as well as genital stimuli (masturbation) or orgasm (Berthier et al., 1987; Calleja et al., 1988) may trigger reflex epilepsy. Only few such cases have been published but this syndrome may be under-reported.

Partial seizures generated from a genital sensory cortical area may result in sensations in the genital organs. Such sensations may be described as clitoral warmth, a hot feeling in the vagina, a pleasant sensation of anal or vaginal constriction or of penetration but also as attacks of actual genital pain. Almost all of the very few described cases have been associated with a parasagittal tumour involving the primary sensory cortex.

Motor symptoms such as erection, lubrication, ejaculation or orgasm may also be a part of an epileptic fit. Such genital events may be experienced by patients as sexual or as non-sexual. Pelvic movements, as a part of epileptic automatisms, or compulsive masturbation in front of other people may occur during or after a seizure.

Sexual phenomena other than sensory events, occurring as part of an epileptic seizure usually feature in patients with complex partial epilepsy, most often with temporal lobe lesions. Sexual automatisms may also occur with frontal lobe lesions. They are very uncommon in primary generalized epilepsy of the grand mal or petit mal type.

Deviant sexual behaviour, such as exhibitionism, fetishism, frotteurism, sadomasochism, transvestism, and violent sexual behaviour or pansexual behaviour, is sometimes displayed by the epileptic patient. Only a small number of cases have been reported but the fact that the behaviour in question may occur episodically and sometimes disappears after treatment favours a causal connection between the behaviour and the epilepsy or the cerebral lesion behind it. In most cases, there were partial complex epileptic seizures and lesions in one or both temporal lobes. Sometimes it can be shown that the deviant behaviour correlated with continuous epileptic discharges in the EEG (psychomotor status). Paranoid delusions of being violated, abused or seduced are not uncommon in epileptic patients (for review, see Lundberg, 1992).

Sexual dysfunction in Parkinson’s disease and other movement disorders

Decrease in sexual desire is common in Parkinson’s disease, especially in women. Symptoms of sexual dysfunction are also frequent in their partners (Brown et al., 1990). Erectile dysfunction during sexual intercourse occurs in half of the men (Koller et al., 1990; Takahashi, 1991; Wermuth and Stenager, 1995) and nocturnal and morning erections are usually absent. Many affected men are also unable to ejaculate and many women are unable to achieve an orgasm. During
Sexual arousal, tremor is frequently enhanced which makes sexual activity more difficult. Muscle rigidity and akinesia may also contribute to difficulties in performance of sexual activities. Patients with Parkinson’s disease are frequently depressed and have a tendency to isolate themselves from other people. A correlation between sexual dysfunction and depression has been observed by some authors. The frequency of sexual dysfunction was similar in patients affected by Parkinson’s disease compared to patients affected by arthritis in one study (Lipe et al., 1990).

The mechanisms behind sexual dysfunction in parkinsonian patients is otherwise not very well understood. Studies of bladder and bowel function have demonstrated a high frequency of bladder detrusor hyper-reflexia and paradoxical contractions of the striated sphincter muscles during defecation, implying specific autonomic nerve damage in these patients (Berger et al., 1987; Singer et al., 1992).

It is interesting to note that decrease of sexual desire is not directly coupled to the severity of the disease. Treatment with dopaminergic compounds may result in an apparent increase, or rather a normalization, of sexual desire without corresponding improvement of the movement disorder. Thus, increase in desire has been reported as an adverse reaction to dopaminergic drugs (Uitti et al., 1989).

The situation is quite different in Huntington’s disease (HD). Fecundity is increased among these patients: those of the family who are going to develop the disease often have more children than those who do not. Increased sexual activity is seen in around 10% of people with HD, sometimes in combination with mania or hypomania. Habitual promiscuity and marital infidelity may be noted at diagnosis of HD. However, HD patients may have difficulty in achieving sexual arousal. Paraphilias such as sexual aggression, exhibitionism and paedophilia have been reported in HD patients (Morris, 1995).

Disorders of sexual inhibition with pansexuality, e.g. copulation with non-living objects, are not infrequent in Tourette’s syndrome (Comings, 1994; Lombroso et al., 1995). Increased sexual activity is also reported in patients with Wilson’s disease (Akil and Brewer, 1995). Impotence is almost universal among patients with multiple system atrophy, both of the striato–nigral type and the olivo–pontocerebellar type. It may be the presenting symptom (Beck et al., 1994; Hodder, 1997).

Sexual dysfunction in multiple sclerosis

Changes in sexual functions are rare at the onset of the disease but become very common during its evolution in both sexes.

In a recent study of 47 women with advanced multiple sclerosis (MS), 60% reported decreased sexual desire, 36% decreased lubrication and 40% diminished orgasmic capacity during the course of the disease. Sensory dysfunction in the genital area was experienced by 62% of the women and 77% had weakness of the pelvic muscles (Hultcr and Lundberg, 1995). In different studies a reduced interest was reported by 29–86% of female MS patients, a reduced sensation by 43–62%, a reduced orgasmic capacity by 24–58%, vaginal dryness by 12–40%, and dyspareunia by 6–40% (see review by Ghezzi, 1999).

Electrodiagnostic data such as cortical evoked potentials of the dorsal nerve of the clitoris (Yang et al. 2000), as well as measurement of vibratory thresholds in the clitoris (Lundberg & Hultcr, unpublished data), imply that pudendal somatosensory innervation is necessary for at least one type of female orgasmic function. To compensate for such a loss, more direct stimulation of the anterior vaginal wall is recommended.

Sexual dysfunction also occurs in early and mild cases of multiple sclerosis. Half of the women in one study of 25 females aged 20–42 years with a low handicap score reported sexual problems. Sensory dysfunction seems to be the most important reason for the sexual problems in these women. Because of severe external dysesthesiae, some patients reported that during a certain period they could not bear direct genital or non-genital contact from their partner. The dysesthesiae were of a maximum intensity from the beginning of an episode of neurological symptoms, but resolved fairly rapidly, as is usual in multiple sclerosis (Lundberg, 1978).

Most patients report a diminished sexual desire during the course of the disease. Some patients may experience a temporary decrease during an episode, in others the problem continues. In certain cases, increased sexual desire has also been described. When this phenomenon is transitory and concurrent with an episode of new symptoms, the hypersexuality might well be the result of a cerebral MS lesion. Other important symptoms of sexual dysfunction in women with multiple sclerosis are deterioration of orgasmic capacity, intensity and quality. In most cases, the orgasmic sensations are reduced. They become shorter, less intense and/or less agreeable. There may be a decrease in orgasmic capacity. These changes may be temporary. However, an orgasmic improvement has also been noticed. The orgasms may be more easily triggered, longer lasting, stronger and more pleasant.

Erectile dysfunction is the most notable sexual dysfunction in men with multiple sclerosis (Vas, 1969; Minderhoud et al., 1984; Valleroy and Kraft, 1984; Kirkeby et al., 1988; Bettis et al., 1994; Ghezzi et al., 1995; Mattson et al., 1995). Figures given in the literature vary between 34 and 80% (see review by Ghezzi, 1999).
Sexual dysfunction in spinal cord disorders

Sexual dysfunction correlates with bladder and bowel sphincter dysfunction, but more mildly with motor and sensory dysfunction in the legs (Hultcr and Lundberg, 1995; Ghezzi et al., 1996; Ghezzi, 1999; Zivadinov et al., 1999). The correlation is poor with disability, clinical course, disease duration. Depression and cognitive impairment play an important role. Anorgasmia has been correlated with MRI brain stem and pyramidal abnormalities as well as with total area of lesions on MRI (Barak et al., 1966).

Changes in sexual functions in MS patients usually start rather abruptly and correlate both with neurological symptoms from the sacral segments and with bladder and bowel dysfunction. Neurophysiological studies may give further indications of involvement of those parts of the nervous system controlling pelvic structures.

Symptoms related to MS, such as fatigue, muscle contractions in the lower limbs, urinary disturbances and the use of aids to manage incontinence, and paroxysmal motor and sensory disturbances triggered by sexual intercourse, can indirectly exert a negative effect on sex life as well as social and physical changes.

Sexual dysfunction in amyotrophic lateral sclerosis

In amyotrophic lateral sclerosis, the neurones of Onuf’s nucleus in the sacral spinal cord innervating the pelvic floor muscles are relatively spared. Sensory and autonomic functions are also unaffected. Thus, patients usually have no difficulty with urination and defecation and normal sexual functions are the rule in males. Despite the fact that severe paralysis of all voluntary movements eventually make intercourse impossible, erection and ejaculation through partner masturbation is possible, and the experience of orgasm is normal (Jokelainen and Palo, 1976).

In Kennedy’s syndrome (X-linked bulbospinal muscular atrophy) gynaecomastia is common, and testicular atrophy, decreased libido and impotence may occur (Ertek and Sirin, 1993; Hokezu et al., 1996).

Sexual dysfunction in spinal cord disorders

Spinal cord injuries. The situation for the tetraplegic and paraplegic patient is well understood because of extensive studies especially of war victims. The effect of the lesion is very much dependent upon its spinal level. If there is a complete destruction of the genital reflex centre in the sacral part of the conus, reflex erection and reflex lubrication occur but there is complete paresis of the striated ejaculatory muscle. Thus, ejaculation is impossible and semen appears as a dribbling from the tip of the penis. In lesions of the upper part of the medulla, reflex erection and reflex lubrication as well as seminal emission and ejaculation may still be possible. However, these patients have impaired sensory perception in the genital organs.

In patients with spinal cord lesion between the level of the lower thoracic segments and the conus, both cerebral and reflex erection and lubrication may be possible, despite the fact that the patient cannot feel the sexual organs. This does not mean that there is no orgasm. A man with a complete lesion of the spinal cord above the conus can never feel the ejaculatory contractions. However, a number of autonomic phenomena being parts of the orgasm can be experienced. In spinal cord lesion there is often a hyperaesthetic area of the body just above or at the segment of the lesion. This is, or may be trained to be, a very strong erogenous zone.

A meta-analysis of 24 studies (Lundberg et al. 2000) of more than 2500 men with spinal cord injuries showed that a median of 80% (range 54–95%) reported erections (any type) without therapeutic assistance. The percentage of SCI men reporting ejaculation without therapeutic assistance was much lower (median 15%, range 0–52%). Fewer (26%) of the patients with complete lower sacral lesions had erectile capacity than those with complete upper cord lesions or incomplete lesions at any level (90–99%) (Bors and Comarr, 1960).

The semen of men with spinal cord injuries is characterized by small volume, low sperm count and low spermatic mobility. This is at least partly dependent on insufficient drainage. Ejaculation can be provoked in many paraplegic males through vibratory stimulation or electrostimulation. It has been shown that repeated vibration-induced ejaculations result in increased semen volume, a larger number of motile sperms and improved sperm penetration capacity. Insemination with autologous semen obtained in such a way has resulted in pregnancies. Collection of semen very early after the spinal cord injury makes it possible to store semen of good quality for future insemination.

A comprehensive review of erectile and ejaculatory dysfunction in spinal cord disorders, and traumatic spinal cord injuries in particular, is given in the International Consultation review by Lundberg et al. (2000).

Women with para- or tetra-plegia are in a better sexual and reproductive situation than men. Deprived of sensation in the sacral segments they may still reach orgasm through stimulation of other erogenous zones, suprasegmental to the lesion, such as breasts, lips, ears...
and so on. Preservation of sensory function in the T11-L2 dermatomes is associated with psychologically mediated genital vasocongestion (Sipski et al., 2001). Deep penetration may provide stimuli enough for orgasm through the sympathetic nervous system or possibly through the vagus nerve. Such women may also have dysmenorrhea. Vaginal stimulation has a strong effect on raising the pain threshold in healthy women. This mechanism may be intact even after complete spinal cord injuries. The majority of para- or tetra-plegic women will continue to menstruate, and may have babies. Sexuality, pregnancy, motherhood and quality of life in women with traumatic spinal cord injuries are reviewed by Berard (1989) and Westgren (1999).

**Spinal cord malformations.** The most important malformation giving rise to sexual dysfunction is meningomyelocele. Dependent upon the degree of the malformation there is a more or less pronounced loss of sexual functions. Some boys have no genital sensations at all, some have erections only and some both erections and emissions. Loss of genital sensations is the major complaint in girls (Dörner, 1977; Wabrek et al., 1978; Sawyer and Roberts, 1999).

In Arnold–Chiari malformation, loss of sexual desire is very common. Some of the men are completely impotent and others have reduced potency. The onset of the sexual complaints nearly always follows the beginning of the neurological disturbances (Caetano De Barros et al., 1975).

**Spinal canal stenosis.** In neurogenic intermittent claudication, some patients note that after walking a short distance an unwanted erection appears, unaccompanied by any libidinous thoughts (Laha et al., 1979; Hopkins et al., 1987). Simultaneously there is pain in the hips on walking radiating to the thighs and legs. The legs tingle and become numb on further walking. If the patients sit down the leg symptoms are relieved and the erection subsides over a few minutes. Erections may also appear after kneeling for 30 min or so. Decompression by bilateral laminectomy results in complete relief of all these symptoms.

**Sexual dysfunction in patients with other forms of myelopathies**

Out of 224 consecutive male patients referred to a sexological outpatient department because of impotence, 17 patients (31–72 years old) were found to have a myelopathy (Brattberg and Lundberg, 1992; Lundberg and Brattberg, 1992). In most of these patients, the neurological disorder was not diagnosed at the time of referral. In those patients in whom the neurological disease was known at the time of investigation, the sexual problem had started with their falling ill, often a very long time previously. The cause was unknown in seven patients; in the remainder the final diagnosis was: postmyelitic (five cases), spinal compression (eight cases), posthaematomyelia (one case), and vitamin B12 deficiency (one case). Morning erections, psychogenic erections and reflex erections were disturbed in most of these men. Disturbances of ejaculation, e.g. retarded ejaculation, total loss of ejaculation and dribbling ejaculation were reported by 10 patients. Seven patients reported disturbances of the experience of orgasm; in one patient, the orgasms were painful.

In one study of about 2000 patients of both sexes with injuries of the cervical spinal cord without paraplegia, 85 reported sexual dysfunction (Perese et al., 1976). Thirty per cent of patients with vitamin B12 deficiency reported sexual dysfunction (Kunze and Leitenmeier, 1976).

**Sexual dysfunction in disorders of the spinal roots and peripheral mononeuropathies in the sacral region**

Our knowledge of sexual function in patients with spinal root disorders or sacral mononeuropathies is mostly based on single case histories or very limited material. A review of such cases will be found in Lundberg (1992).

Many patients with sacral root lesions are distressed by pain at coitus. Ejaculation may also be painful. Impotence occasionally occurs. As bilateral loss of function is rare some kind of sexual gratification is usually possible. Ejaculation may be delayed. Bilateral damage to all S2-5 roots or nerves results in dribbling ejaculation, because seminal emission is preserved, but paresis of bulb- and ischio-cavernous muscles is present. In such a case, reflex erection is not possible but psychogenic erection mechanisms are still active. Unilateral loss of all sacral nerves on one side results in ipsilateral genital anaesthesia. However, sexual function is usually not impaired, because the innervation of the other side is sufficient for normal genital reflex responses.

Peripheral mononeuropathies of the pudendal nerve or branches of that nerve in particular are not uncommon, especially in women. These nerve lesions frequently result in so much pain and dyspareunia that coitus becomes impossible or at least unpleasant.

**Sexual dysfunction in polyneuropathies**

*Diabetes mellitus.* The prevalence of impotence in male diabetics has always been reported to be high. In reviewing six previous studies comprising a total of 1619 cases Neubauer (1971) noted figures of between 39 and 75% (mean 55%). Later investigations have
found similar results (Ellenberg, 1971; Kolodny et al., 1974; Jensen, 1981; Fairburn et al., 1982). In one study with a healthy control group the difference was remarkable, 34% vs. 0% (Jensen, 1981). Retrograde ejaculation is reported in diabetic patients as a result of paresis of the internal bladder sphincter. In most studies only a few cases have been identified (Greene et al., 1963; Ellenberg and Weber, 1966; Schirren et al., 1973). However, systematic searches for this symptom using the proper questions has given figures as high as 14% (unpublished observation).

A dissociation between different types of erectile failure is often found. More patients seem to have absent or rare morning erections and absent or weak erections on visual stimulation than absent or weak erection on genital stimulation. In sleep laboratory studies (Karacan et al., 1977, 1978; Hirshkowitz et al., 1990) on men with diabetic polyneuropathy, fewer sleep-related erections, shorter tumescence time, diminished penile circumference increase and lower penile rigidity were recorded in those with diabetic polyneuropathy than in non-diabetic men. Much less is known about sexual desire in diabetic men (Jensen, 1981).

A correlation between impotence and the occurrence of peripheral neuropathy is sometimes reported (Ellenberg, 1971; Kolodny et al., 1974; Jensen, 1981; Lehman and Jacobs, 1983). A correlation between impotence and autonomic bladder dysfunction in diabetic patients has also been described (Ellenberg, 1971; Buvat et al., 1985; Ertelkin et al., 1989). However, to analyze a diabetic autonomic polyneuropathy, it is not enough to study just the somatic nerves in the legs.

Histological and histochemical studies of the autonomic nervous system have been performed in a number of men with diabetic impotence. The content of norepinephrine in the corpora cavernosa was found to be significantly lower in insulin-dependent and diet-controlled diabetic men than in non-diabetic men. Neither changes in choline acetyltransferase activity nor morphological alterations of the nerve fibres of erectile tissue were observed (Melman et al., 1980a; 1980b). Using an isotope technique, both choline accumulation and acetylcholine synthesis and release were significantly reduced in penile tissue from impotent diabetic patients compared to that from impotent nondiabetic patients. The impairment in acetylcholine synthesis worsened with the duration of the diabetes (Blanco et al., 1990). Morphological changes have been demonstrated in unmyelinated nerve fibres in the penis (Faerman et al., 1974).

Nitric oxide is considered to be the most important factor in relaxing corpus cavernosum smooth muscle, thus giving rise to erection (for review, see Andersson et al. 2000). Hyperglycaemia (and some glycosylation products) promotes the chemical inactivation of NO (Brodsky et al. 2001). There seems to be a selective nitricergic neurodegeneration in diabetes (Cellek et al., 1999). This may be an important mechanism behind erectile dysfunction in diabetic men.

In addition, a number of physiological and neurophysiological tests have been applied. Cardiovascular reflex tests exploring the sympathetic nervous system cannot be used to differentiate between diabetic men with erectile failure and those without this problem (Quadri et al., 1989). On the other hand, measurement of bulbocavernosus and urethral reflex latencies as well as penile evoked potentials have shown a significantly higher number of abnormalities in impotent diabetic males than in impotent non-diabetic males and potent diabetic males (Bemelmans et al., 1994).

Studies of sexual function in women with diabetes mellitus have given conflicting results. In one study 35% of the diabetic women were reported to have had orgasmic dysfunction in the preceding year as compared to 6% of the controls (Kolody, 1971). In another study the frequency of sexual dysfunction was around 25% in both insulin-treated diabetic women and in age-matched controls (Jensen, 1981). An important negative impact on sexual life measured as problems with desire, activity, lubrication, orgasmic capacity, satisfaction and on the relationship with the sexual partner compared to matched control women was found only in type II diabetic women (Schreiner-Engel et al., 1987); not in type I. Loss of libido has been reported in some other studies (Newman and Bertelson, 1986; Campbell et al., 1989).

In a recent structured interview study, Hulter et al. (1998) found that 26% of 42 women with insulin-dependent diabetes had a decreased sexual desire, 22% had decreased vaginal lubrication and 10% had decreased capacity to acquire orgasm. Several of the women reported more than one dysfunction. Taken together the figure for sexual dysfunction was 40%. Among age-matched controls without diabetes or any neurological disease, only 7% of the women reported some kind of sexual dysfunction.

Lubrication, the most important female counterpart to penile erection in males, is otherwise rarely studied. Tyrer et al. (1983) found that in insulin-dependent diabetic women vaginal lubrication was frequently inadequate or required prolonged stimulation compared to controls. There are two psychophysiological studies in women with diabetes mellitus. One of them did not show any difference compared to controls (Slob et al., 1990). In the other, diabetic women were found to experience significantly less physiological arousal to erotic stimuli than controls (Wincze et al., 1993).
A number of autonomic and sensory symptoms, such as reduced foot perspiration, increased gustatory perspiration and impaired subjective vulvar sensibility, were noted more frequently by women with insulin-dependent diabetes than by controls (Hulter et al., 1996). The diabetic patients had significantly higher vibration perception thresholds in the hands and in the clitoris than the controls. Reduced foot perspiration, increased gustatory perspiration, constipation and incontinence correlated with sexual dysfunction.

A postmortem study of tissue samples from 17 diabetic women (Zrustová et al., 1978) showed evidence of both clitoral nerve degeneration and changes in blood vessels in the clitoris. A non-diabetic control group did not show any signs of neuropathy or vascular damage. However, so far, this study does not seem to have been replicated.

It should be noticed that sexual problems in patients with diabetes mellitus may be caused by many different mechanisms besides polyneuropathy. The metabolic process in itself, with variations in blood sugar and acidosis certainly plays a role. It is not believed that other endocrine insufficiency such as hypogonadism plays an important role in either the low sexual desire or the erectile dysfunction. Vascular damage to small vessels as well as in larger arteries may result in decreased blood flow to the cavernous tissues in both sexes. Two comprehensive reviews have recently been published about men (Ertekin, 1998) and women (Enzlin et al., 1998) with diabetes.

**Other polyneuropathies**

Autonomic dysfunction, including sexual dysfunction, is a common complication in peripheral neuropathies (McDougall and McLeod, 1996). Polyneuropathies due to vitamin deficiency (Vitamin B1 Tjandra and Janknet, 1997; Vitamin B12 Kunze and Leitenmajer, 1978) or plasma cell dyscrasia (Takatsuki and Sanada, 1983) may cause erectile dysfunction.

Very little has been written about sexual dysfunction in hereditary polyneuropathies. However, based on physiological data, impotence, decreased lubrication, retarded or retrograde ejaculation and orgasmic difficulties are to be expected. Thus, impotence and ejaculation problems have been observed in patients with Guillain-Barré syndrome, Charcot-Marie-Tooth syndrome (Bird et al., 1994; Crabtree, 1997), adrenomyeloneuropathy/adrenoleukodystrophy (Sakakibara et al., 1998; Garside et al., 1999), Refsum’s disease (Lundberg, unpublished observation), Friedreich’s ataxia, Riley-Day syndrome, HSAN I-IV (four types of hereditary sensory and autonomic polyneuropathy) and primary amyloidotic polyneuropathy (Andersson and Hofer, 1974; Obayashi et al. 2000). In a study of 341 consecutive patients with erectile dysfunction, neurophysiological evaluation for polyneuropathy revealed the presence of polyneuropathy in 38% of diabetic cases and 10% of impotent cases of other aetiology (Vardi et al., 1996). The adrenoleucodystrophies represent a group of patients of particular interest because of the severe prognosis of this disease and the predominance of CNS lesions (Powers and Schaumberg, 1980). It does not seem to be the involvement of the somatic nerves (pudendal nerves) that is of importance in the hereditary motor and sensory neuropathies in causing impotence (Vodusek and Zidar, 1987).

**Myopathies**

In certain types of progressive muscular dystrophies, myotonic dystrophy (Marinkovic et al., 1990; Mastrogiacomo et al., 1994; Olsson et al., 1996), the Becker type (Hallen, 1971) and ocular myopathy of the autosomal progressive external ophthalmoplegia type (Lundberg, 1966; Melberg et al., 1996) in particular, hypogonadism in combination with disturbances of erectile function and desire has been described. In females, secondary amenorrhoea is common. Impotence and amenorrhoea may also occur in mitochondrial encephalomyopathies such as MERFF and MELAS syndromes (Chen and Huang, 1995).

**Sexual dysfunction and prescription drugs**

**Antidepressant drugs.** For the non-selective monoamine reuptake inhibitors, impotence, decreased desire and problems with ejaculation are the most frequent unwanted sexual effects. Problems within the orgasmic phase of the sexual response cycle are more prevalent for the group of selective serotonin reuptake inhibitors (SSRIs) than for the group of non-selective monoamine reuptake inhibitors (Kimura et al., 1984; Patterson, 1993; Montejo-González et al., 1997; Lundberg and Biriell, 1998). The most frequent adverse reactions with SSRIs are decreased desire and the most typical are anorgasmia in females and problems with ejaculation and anorgasmia in males. Impotence is less frequently reported with the group of SSRIs than for the group of non-selective monoamine reuptake inhibitors. Trazodone is the antidepressant drug with the highest number of reports of priapism (Saitz de Tejada et al., 1991; Lundberg and Biriell, 1998; Lundberg 2000). Priapism caused by this drug is also recorded in women.

**Antihypertensive drugs.** The greatest number of sexual adverse drug reaction reports concern antihypertensive drugs (Lundberg and Biriell, 1993). All classes among these drugs are represented. The different drugs seem to have few pharmacological effects in common.
besides lowering the blood pressure. Hence, the impotence is probably vascular. However, because decrease in libido is also reported with these drugs, this effect may be partly central. Alpha-adrenoreceptor blocking agents as well as alpha- and beta-adrenoreceptor agents and guanidine derivatives have been reported in connection with ejaculation failure. Priapism has been reported with alpha-adrenoreceptor blocking agents (such as prazosin).

Other types of drugs. Other types of drugs of importance in this context are hormonal contraceptives for systemic use, anti-epileptic drugs, dopaminergic drugs, antipsychotic drugs and anxiolytic drugs. Hormonal contraceptives for systemic use are reported to cause decrease in sexual desire. Anti-epileptic drugs frequently decrease sexual desire and cause impotence. However, it is difficult to evaluate what is cause by the underlying brain disorders in itself and what is caused by the drug in question (see paragraph on epilepsy). Dopaminergic drugs (L-dopa, bromocriptine, selegiline) represent the only group more frequently associated with increased desire than with decreased desire (see above) (Hyyppä et al., 1975). Antipsychotic drugs with alpha-adrenoreceptor blocking properties, particularly chlorpromazine, thioridazine, haloperidol and clozapine, have been reported to cause priapism and also ejaculation failure. These drugs may also cause painful, retrograde or spontaneous ejaculations (Keitner and Selub, 1983; Sitsen, 1988).

Treatment and counselling strategies for sexual dysfunction in neurological disorders

General treatment principles
Sexual counselling, discussion and communication with the patient and their partner about their sexual life is an important part of the rehabilitation strategy in neurological disorders. It should be recognized that sexual dysfunction may be the first symptom of a neurological disorder. The first step is to let the patient know that it is permitted to discuss sexuality in the clinical setting. The next step is to give limited information about sexual physiology and practical issues that are pertinent to a person with the particular handicap and symptomatology in question. Specific suggestions about therapeutic methods and strategies may then follow. In a limited number of cases, there is also a need for intensive therapy under the supervision of a psychotherapist trained in neurosexology. It can be combined with sensate focus exercises. Here body awareness exercises and psychotherapy are merged.

Intracavernous injection as a treatment for neurogenic impotence
Intracavernous injection (ICI) of vasoactive substances has become a standard treatment procedure in erectile dysfunction of organic causes for the last decade. In neurology, it has mostly been used in men with spinal cord injuries or multiple sclerosis (Beretta et al., 1986; Bodner et al., 1987; Sidi et al., 1987; Kirkeby et al., 1988; Costa et al., 1993; Hirsh et al., 1994).

Originally papaverine was used but this drug has largely been replaced by prostaglandin E1. In neurogenic impotence, rather low doses of PGE 1 are needed, 2.5 µg up to a maximum of 10 µg. In arteriogenic impotence, higher doses are needed. The effect is very rapid and may last for 2–4 h. Longer-lasting erection should be treated as priapism (see below). Haematological malignancies and anticoagulant therapy are contraindications. Local bleeding and pain are common side-effects, and fibrosis may develop in the corpora cavernosa leading to loss of effectiveness. Moxisylylate, an alpha-blocking agent has been studied against placebo in spinal cord-injured patients (Costa et al., 1993) with rather good results. However, long-term studies with this particular drug are lacking.

The drugs should be tested during medical supervision, then a suitable dose can be self-administrated by the patient or his partner.

Prostaglandin E1 can also be administered as a gel intraurethrally (MUSE). This is more practical but less effective than ICI (Padma-Nathan et al., 1997; Bodner et al., 1999).

Oral treatment in patients with neurogenic impotence
As mentioned above, a number of oral prescription drugs may have the potential to be used to treat impotence. However, as most of these drugs act centrally, they are not very effective in this regard and have a number of other side-effects. Recently a specific, peripherally acting vasodilatation agent, sildenafil (Viagra), has become available. This is a specific phosphodiesterase-5 inhibitor. One hour before desired sexual activity, 25, 50 or 100 mg can be given orally. It has a very discrete spontaneous effect but it enhances erection mechanisms only if the individual is sexually stimulated. Sildenafil taken at bedtime significantly increases nocturnal erections (Montorsi et al., 2000).

Sildenafil can be used repeatedly with only minor problems. However, it should be used with great care in the cardiac patient and is contraindicated in combination with vasodilatation drugs of the nitro type (Boolell et al., 1996; Goldstein et al., 1998). Neurological disorders with a disturbed vasoregulation may also be a contraindication. The most common adverse events are otherwise headache and dyspepsia. Ischaemic optic neu-
Erection occurs within 10–25 min. Nausea is the most common adverse reaction (Heaton, 2000).

(A) Central Agents
- i-Adrenergic receptor antagonists
  - Phentolamine
  - Delquamine
  - Yohimbine
- ii-Dopamine receptor agonists
  - Apomorphine
  - Bromocriptine
- iii-Serotonergic receptors agonist
  - Trazodone
(B) Peripherally acting agents
- Nitroglycerine
- Phosphodiesterase-5 inhibitors (Sildenafil and others)
  - l-Arginine
  - Minoxidil

II. Intracavernosal therapy
- Papaverine
- Papaverine-phenolamine mix
- Prostaglandine E1
- Calcitonin Gene-related Peptide (CGRP)
- Linsidomine
- Trimix (Papaverine-Phentolamine-Prostaglandin E1)
- Vasoactive intestinal peptide (VIP)

III. Penile vascular surgery

IV. Penile prosthesis

V. Penile vacuum devices

Table 2 Therapeutic methods in impotence of organic causes

<table>
<thead>
<tr>
<th>I. Oral and topical pharmacotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Central Agents</td>
</tr>
<tr>
<td>i-Adrenergic receptor antagonists</td>
</tr>
<tr>
<td>Phentolamine</td>
</tr>
<tr>
<td>Delquamine</td>
</tr>
<tr>
<td>Yohimbine</td>
</tr>
<tr>
<td>ii-Dopamine receptor agonists</td>
</tr>
<tr>
<td>Apomorphine</td>
</tr>
<tr>
<td>Bromocriptine</td>
</tr>
<tr>
<td>iii-Serotonergic receptors agonist</td>
</tr>
<tr>
<td>Trazodone</td>
</tr>
<tr>
<td>(B) Peripherally acting agents</td>
</tr>
<tr>
<td>Nitroglycerine</td>
</tr>
<tr>
<td>Phosphodiesterase-5 inhibitors</td>
</tr>
<tr>
<td>l-Arginine</td>
</tr>
<tr>
<td>Minoxidil</td>
</tr>
</tbody>
</table>

III. Penile vascular surgery

IV. Penile prosthesis

V. Penile vacuum devices

Therapeutic methods in impotence of organic causes

I. Oral and topical pharmacotherapy

(A) Central Agents
- i-Adrenergic receptor antagonists
  - Phentolamine
  - Delquamine
  - Yohimbine
- ii-Dopamine receptor agonists
  - Apomorphine
  - Bromocriptine
- iii-Serotonergic receptors agonist
  - Trazodone
(B) Peripherally acting agents
- Nitroglycerine
- Phosphodiesterase-5 inhibitors (Sildenafil and others)
  - l-Arginine
  - Minoxidil

II. Intracavernosal therapy
- Papaverine
- Papaverine-phenolamine mix
- Prostaglandine E1
- Calcitonin Gene-related Peptide (CGRP)
- Linsidomine
- Trimix (Papaverine-Phentolamine-Prostaglandin E1)
- Vasoactive intestinal peptide (VIP)

III. Penile vascular surgery

IV. Penile prosthesis

V. Penile vacuum devices

Surgical procedures and technical devices

Surgical revascularization in traumatic cases and severe local arteriosclerosis is of limited importance in the neurological patients. So are also procedures to treat cavernous insufficiency (venous leakage). Penile prosthesis, implantation of semifirm or inflatable rods have frequently been used during the past decades. However, these techniques have so many disadvantages and complications that they are rarely to be recommended nowadays when oral medications and ICI are available. However, penile vacuum devices and penile rings still have a place in the treatment of impotent neurological patients (Heller et al., 1992; Rivas and Chancellor, 1994; Denil et al., 1996; Seckin et al., 1996).

Treatment of anejaculation

In cases of anejaculation/anorgasmia, vibratory stimulation may be helpful (Brindley, 1981). The presence of intact dorsal penile nerves is necessary for the ejaculatory response to penile vibratory stimulation (Wieder et al. 2000). If the aim is to retrieve sperm for in vitro fertilization or intracytoplasmic sperm injection, electroejaculation is preferred (Sato, 1991). Such treatment should preferably be supervised by experienced specialists. For that reason, details will not be given in these guidelines. A comprehensive description can be found in two recent reviews (Kamischke and Nieschlag, 1999; Lundberg et al., 2000).

Treatment of priapism

Priapism caused by a spinal cord disorder or appearing as an adverse drug reaction usually has a good prognosis with conservative treatment. Painless priapism of less than 6 h duration should be treated at first by cooling (Bondil et al., 1997; Lundberg, 2000). In the case of failure or if the priapism is painless but has been more than 6 but less than 24 h in duration, intracavernous injection of an alpha-adrenergic agonist such as metaraminol is recommended. In painful priapism or when the other conservative methods have failed, penile puncture should be used. Few cases of this type of priapism need open surgery. When ICI or puncture is performed, it is recommended to draw a cavernosal blood sample for blood gas analysis to evaluate cavernosal anoxia.

Treatment of lack of sexual arousal and anorgasmia in women

Postmenopausal women as well as women showing signs of oestrogen insufficiency should be given hormone replacement therapy. Androgens may also be supplemented in women with no risk of being pregnant. Otherwise, there is at present no drug treatment with proven effect available. Counselling according to the first three steps of the PLISSIT model should be followed. Vibratory stimulation may be very helpful both in patients with genital sensory disturbances and those with paresis and movement disorders. The vibrators should preferably be applied against the clitoris.
Dildos of various types, also in combination with vibration, are sometimes very useful.

**Treatment of reduced or increased sexual desire**

Hormone insufficiency, testosterone in men and oestrogens in women, should always be corrected. Testosterone may also be helpful in women, but cannot very often be used in fertile women because of the risk of masculinization. Hyperprolactinaemia should be treated with bromocriptine or similar. Dopaminergic drugs may be tried in certain cases with reduced desire. However, the drug of choice in women with low sexual desire is still to be found.

Increased sexual desire that has to be treated is rare. Androgen antagonists (cyproterone acetate, medroxyprogesterone acetate) may be effective. In severe cases, neuroleptics may be tried.

**Conclusions and recommendations**

Sexual disabilities such as loss of sexual desire, erectile dysfunction or decreased lubrication and sexual arousal, as well as disturbances of ejaculation and orgasm, are very common among patients with neurological disorders or those suffering from sequelae of injuries. In brain disorders and after brain injuries, sexual desire may be reduced and behavioural disturbances may occur. Sexual adverse reactions have been reported with the use of many prescription drugs acting on the nervous system. Sexual disabilities may be the presenting symptom or one of the early symptoms of a neurological disorder.

All neurological patients should have the opportunity of sexual counselling. The majority of them, even those with complete spinal cord injuries, can be treated for erectile and ejaculatory dysfunction.

**Diagnosis**

A careful case history should be taken and the neurological examination should include the sacral segments. In selected patients (particularly those with suspected peripheral nervous system involvement), neuropsychological tests, should, in addition to other indicated investigations, be considered in patients seeking medical advice because of a sexual disability.

**Treatment**

1. **Permission:** The first step of the counselling is to open the mind of the patient to the existence of sexual disabilities.
2. **Limited information:** The second step is to give the patient proper information about sexual issues in this particular type of disorder/injury.
3. **Specific suggestions:** Practical information about positions and stimulation techniques (vibrators) and technical aids and devices (vacuum extraction devices) should be given.
4. **Intensive therapy:** The next step is to use specific medical as well as surgical, treatment available, for the different types of problems; such as decrease in desire, erectile dysfunction, problems with sexual arousal in women as well as ejaculatory dysfunction and orgasmic problems. These treatments include oestrogen substitution in females, testosterone substitution in both sexes, intracavernous injection of prostaglandin E1, papaverine or moxisylyate, transdermal or intraurethral application of different drugs, oral administration of phosphodiesterase-5 inhibitors such as sildenafil and, in a limited number of cases, penile prosthesis. Treatment of bladder dysfunction and spasticity as well as autonomic dysreflexia is also important.
5. **In spinal cord injuries, semen can be retrieved by the use of assisted ejaculation methods such as penile vibratory stimulation (PVS) or rectal probe electroejaculation (EEJ). PVS should be used first due to its safety, reliability and low investment in time and money. It also results in better semen quality. If PVS fails, the patient should be referred to a specialist centre for EEJ. So far, there are no treatments to normalize semen quality in men with spinal cord injury, although semen quality does not improve when EEJ is used.**

**References**


Benelmans BLH, Meuleman EJH, Doesburg WH, Notermans SLH, Debruyne FMJ (1994). Erectile dys-


© 2001 EFNS European Journal of Neurology 8 (Suppl. 3), 2–24.


